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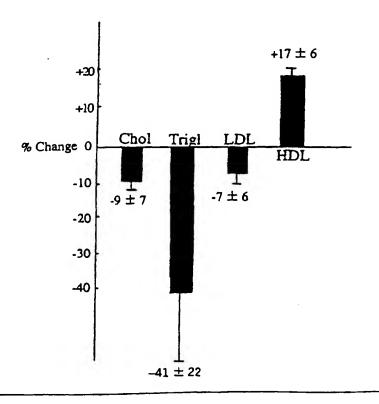
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(54) Title: FISH OIL AND GARLIC NUTRITIVE COMPOSITION

(57) Abstract

The present invention relates to nutritional supplements to the human diet used to increase levels of HDL, and decrease levels of O-LDL, cholesterol, and triglycerides in human blood plasma. More specifically, the present invention teaches a novel nutritional supplements which contain a novel combination of fish oil, garlic, rutin, and capsaicin, as well as methods of preparing the nutritional supplements.

Effect of Fish Oil/ Garlic on Lipid Profile



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FISH OIL AND GARLIC NUTRITIVE COMPOSITION

Cross-Reference to Related Application

This is a continuation-in-part of co-pending provisional application Ser. No. ______, filed March 12, 1996.

BACKGROUND OF THE INVENTION

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Field of the Invention

The present invention provides a novel composition for preventing cardiovascular diseases in the human system, and more specifically to nutritive compositions containing fish oil, garlic, rutin, and capsaicin that reduce the levels of triglycerides, cholesterol, and low density lipoprotein (LDL) in the human blood serum, and increase the levels of high density lipoprotein (HDL) in human blood serum.

2. Background of the Invention

In the last few years, scientific literature has provided strong evidence for a bona fide link between micronutrient compositions (such as vitamins, minerals, fish oils, and plant extracts) and cardiovascular disease. For humans of high risk for cardiovascular diseases, realizing an appreciable reduction in the levels of high cholesterol, triglycerides, low density lipoprotein (LDL) in their blood serum is known to be important for reducing the risk of cardiac diseases. It is also known that effecting an increase in the levels of high density lipoprotein (HDL) also provides a significant decrease to the risk of cardiac diseases.

Cardiovascular disease resulting from the buildup of arterial plaque is known to be a leading cause of illness and

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Arterial plaque is caused by precipitous death in humans. material formed chiefly of oxidized low density lipoprotein (O-LDL). The buildup of plaque in the form of O-LDL in the arteries is understood to be a factor in ischemic heart disease. radical oxidants, many of which come from naturally occurring sources such as sun exposure, metabolism of certain nutrients, exercise, or are otherwise often observed in persons suffering from diabetes and high blood pressure, act to oxidize LDL into its deleterious form, O-LDL. Free radical "scavengers" such as vitamins A, E, C, and selenium are believed to react with these oxidants and render them incapable of oxidation. The inhibitory action of these antioxidants thus inhibits the formation of O-LDL, thereby lowering the levels of arterial plaque deposits in In contrast, the presence of high density blood vessels. lipoprotein (HDL) in the body is understood to have beneficial health effects. Specifically, HDL is known to be a more soluble form of lipoprotein, hence its presence does not significantly contribute to the formation of arterial plaque. In addition, it is known that HDL is able to absorb plaque material and may thus directly reduce the amount of arterial plaque.

3. Description of Prior Art

Essential fatty acids (EFAs) are naturally occurring unsaturated fatty acids with a chain length of 18, 20, or 22 carbon atoms. These EFAs cannot be synthesized by the body, hence, dietary intake of EFAs is required. Two fatty acids which fall within the family of EFAs are eicosapantaenoic acid (EPA) and docosahexaenoic acid (DHA), both of which are commonly found

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in fish oils. Epidemiological observations indicate that fish oils reduce platelet aggregation and serum triglycerides which may reduce the risk of myocardial infarction, hypertension, atherosclerosis, and certain types of cancer. [Gerster, H., Internat. J. Vit. Nutr. Res., 65:3-20 (1994)]. Specifically, it has been shown that EPA and DHA derived from fish oils play important structural roles in membranes of most cells, and influence the fluidity of the cell membranes as expressed by decreased whole-blood viscosity and increased erythrocyteflexibility and deformability [Gerster, cited above]. addition, EFAs such as EPA and DHA are known precursors of eicosanoids -- a class of compounds which includes prostanoids such as prostaglandins and thromboxanes, leukotrienes, and hydroxy fatty acids. Eicosanoids are known are known to affect platelet aggregation, permeability and tone of the blood vessel walls, blood pressure, and inflammatory immune reactions. [Gerster, cited above].

Fish oil dietary supplementation is known to have other beneficial health effects. Glycogen storage disease is an inherited disorder, and is often complicated by severe hyperlipoproteinemia and hypercholesterolemia, which increase the risk of premature atherosclerosis and cardiovascular diseases. It has been reported that patients suffering from glycogen storage disease that received 10 grams of fish oil for 3 months experienced a significant decrease in levels of triglycerides in the blood serum (-49%) and cholesterol levels in the blood serum (-23%), and a reduction in LDL levels in the blood serum (-40%), and a significant increase in HDL levels in the blood serum

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(+30%). [Levy, E., et al., <u>I. Am. J. Clin. Nutr.</u>, <u>57</u>:922-29

Garlic powder has been proposed to have a number of valuable as a preventative against human body the cardiovascular diseases. For example, daily ingestion of garlic leads to reduced levels of lipids in human blood serum, increased fibrinolysis and tissue plasminogen activator (t-PA) activity, and decreased plasma fibrogen viscosity, each of which may lessen [Brosche, T. et al., the likelihood of cardiovascular disease. British J. Clin. Practice, Supp. 69:12-19 (1990); Kiesewetter H. et al., British J. Clin. Practice, Supp. 69:24-29 (1990)]. addition, the daily ingestion of garlic is known to reduce the total levels of cholesterol and triglycerides in human serum, as well as reduce blood pressure peripheral vasodilation. W. et al., <u>British J. Clin. Practice</u>, <u>Supp. 69</u>:3-6 (1990)].

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Flavonoids are secondary metabolites which are found in edible plants and foodstuffs derived from plants. Flavonoids are widely recognized as having antiallergic, anti-inflammatory, antiviral, antiproliferative and anticarcinogenic activities.

[Manach, C., et al. J. Nutr., 125:1911-22 (1995)]. Among flavonoids, flavonols occur most abundantly in plants as possess most of these biological properties. [Manach, cited above]. Flavonols naturally occur as 0-glycides, typically having a sugar moiety bound at the C-3 position. Rutin is the principal glycoside form of quercetin, the most abundant flavonol in fruits and vegetables.

Capsaicin is a prominent chemical entity in plants of the Capsicum genus, which include chili peppers, red pepper, and

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paprika. Capsaicin is actually a class of compounds of branched-and straight-chain alkyl vanillylamides. The antimicrobial and analgesic properties of capsaicin have been known for centuries. In addition, capsaicin-containing products have been used to treat rheumatoid arthritis, osteoarthritis, diabetic neuropathy, postherpetic neuralgia, postmastectomy pain syndrome, cluster headache, and reflex sympathetic syndrome. [Cordell, G. and Araujo, O., Ann. Pharm., 27:330-36 (1993)].

Although compositions used to reduce the risks of cardiovascular disease are known, the present invention comprises a novel combination of fish oil, garlic, rutin, and capsaicin, which achieve this purpose. As such, there remains a need in the art for novel compositions like those of the present invention which may be used to treat or prevent cardiovascular disease and disorders.

SUMMARY OF THE INVENTION

The present invention relates to the use of nutritional supplement compositions to overcome the nutritional deficiencies typically associated with the normal Western diet. The compositions of the present invention are obtained by combining fish oil, garlic powder, rutin, and capsaicin. Specifically, the present invention relates to the daily co-administration of one preparation of fish oil, preferably as a single fish oil lozenge, and a preparation comprised of garlic powder, rutin, and capsaicin, preferably in a single lozenge.

It is therefore an object of the invention to provide nutritious and safe compositions for human consumption as dietary

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supplements that contain fish oil, garlic powder, rutin, and capsaicin.

It is another object to provide novel compositions which will increase the levels of HDL in human blood serum.

It is a further object of the invention to provide compositions which will decrease levels of O-LDL in human blood serum.

It is still another object of the invention to provide compositions which will reduce the levels of cholesterol and triglycerides in human blood serum.

The increase of HDL and the reduction of cholesterol and O-LDL should act to reduce the risk of heart disease in humans. Therefore, it is another object of the present invention to provide for the reduction of the risk of cardiovascular disease by daily administration of the compositions of the invention.

DETAILED DESCRIPTION OF THE INVENTION

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Daily doses of the compositions of the present invention are aimed at reducing the rate of occurrence of heart disease and are comprised of: (1) fish oil; (2) garlic powder; (3) rutin; and (4) capsaicin. More specifically, the compositions of the present invention are a combination of a fish oil preparation, preferably in the form of a single fish oil lozenge, and a preparation comprised of garlic powder, rutin, and capsaicin, preferably in the form of a single lozenge which is co-administered with the fish oil lozenge. The preferred weight of the fish oil lozenge is between about 500 mg and about 1500 mg, preferably about 1000 mg. The preferred weight of the garlic lozenge is between about

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400 mg and about 1000 mg, and most preferably about 700 mg.

The fish oil preparation component of the compositions of the present invention may be available from commercial sources. [Arista, Pharmachem]. EPA and DHA are the active moieties of the fish oil preparation. The fish oil preparation of the present invention comprises EPA in the amount of about 250 mg to about 350 mg, and most preferably about 300 mg. The remainder of the fish oil preparation comprises from about 150 mg to about 250 mg of DHA, and preferably about 200 mg of DHA. The total weight of the fish oil preparation of the present invention is from about 500 mg to about 1500 mg, and preferably about 1000 mg per fish oil lozenge when in the form of a single fish oil lozenge.

The garlic powder used in the garlic powder, rutin, and capsaicin preparation component of the compositions of the present invention may be obtained from commercially available sources. [Extracts, Ashland, Pure-Gar]. In addition, it is preferable to use a deodorized and aged form of garlic powder. A pharmaceutically acceptable form of garlic powder used in the compositions of the present invention comprises, by weight, from about 100 mg to about 700 mg, and more preferably about 175 mg to about 650 mg, and most preferably 500 mg of deodorized and aged garlic powder per garlic/rutin/capsaicin lozenge when in the form of a single lozenge.

The rutin which is employed in the garlic powder, rutin, and capsaicin preparation component of the compositions of the present invention may also be obtained from commercially available sources. [Westco Chemical, Freeman Industries, Inc.]. The rutin component of the garlic powder, rutin, and capsaicin

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preparation comprised, by weight, from about 10 mg to about 150 mg, and most preferably about 100 mg.

Capsaicin which is used in the compositions of the present inventions may be commercially obtained. [AllChem, Good Hope Botanicals]. When employed in the garlic powder, rutin, capsaicin preparation of the present invention, the capsaicin component of the compositions of the present invention comprises, by weight, from about 20 mg to about 150 mg, and most preferably about 100 mg of capsaicin.

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The garlic powder, rutin, and capsaicin components are admixed in the same preparation. This preparation is co-administered with the fish oil preparation -- the two preparations comprising the compositions of the present invention.

These preparations may be made by conventional methods. prepare the compositions of the invention, the above-described fish oil and garlic powder/rutin/capsaicin preparations are combined as the active ingredient in intimate admixture with a compounding conventional according to carrier suitable This carrier may take a wide variety of forms techniques. desired preparation of form the upon depending administration, e.g., oral, sublingual, nasal, or parenteral.

In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed. For oral liquid preparations (e.g., suspensions, elixirs, and solutions), media containing for example, water, oils, alcohols, flavoring agents, preservatives, coloring agents and the like may be used. Carriers such as starches, sugars, diluents, granulating agents,

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lubricants, binders, disintegrating agents, and the like may be used to prepare oral solids (e.g., powders, capsules, pills, tablets, and lozenges). Lozenges are a preferred oral dosage form. Controlled release forms may also be used. Because of their ease in administration, lozenges, tablets, pills, and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar coated or enteric coated by standard techniques.

Examples of these additional inactive components which provide for easier oral administration include but are not limited to lemon bioflavonoids [Botanical International, Freeman], parsley powder, d-alpha tocopherol, bee's wax, lecithin, gelatin, purified water, and glycerin. These compounds may be used in creating the lozenges of the novel nutritional supplements.

For parenteral products, the carrier will usually comprise sterile water, although other ingredients may be included, e.g., to aid solubility or for preservation purposes. Injectable suspensions may also be prepared, in which case appropriate liquid carriers, suspending agents, and the like may be employed.

A preferred method for using the present invention is for the user to ingest, daily from about 4 to 8 lozenges of the fish oil preparation, most preferably about 6 lozenges of the fish oil preparation, together with from about 3 to 5 lozenges of the garlic powder, capsaicin and rutin preparation, and most preferably 4 lozenges of the garlic powder, capsaicin and rutin preparation.

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The following examples illustrate the preferred embodiments of the present invention. These examples are illustrative only, and do not purport to limit the invention in any fashion.

EXAMPLE 1

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The effect of the present invention on the human lipid profile was measured. A double blind study carried out at the University of California at Irvine Medical School showed that the proper use of the present invention provides for the following effects in human blood serum: (1) a significant reduction in triglyceride levels; (2) a significant decrease in cholesterol and LDL; and (3) a significant increase in the levels of HDL.

The protocol followed during this investigation was as follows. Ten subjects participated in a month-long study wherein each subject ingested ten lozenges for each day of the study. The placebo group used 10 nonactive lozenges each day for one month, and the active group ingested 10 lozenges of the present invention each day for one month. Each subject ingested three fish oil lozenges and two garlic powder/rutin/capsaicin lozenges (twice daily) for a total daily ingestion of ten lozenges. identity of the lozenge was unknown by the subjects, and to the Blood double blind study). а (i.e., examiner (approximately 4 cc) was collected at the starting time and again after the completion of one month of usage. A fasting lipid profile was conducted on the plasma samples using a lipid fractionation panel automated system. [Hewlett-Packard Co.]. In addition, measurements of electrolytes (including calcium ion) and glucose levels were made using the Chem 18 automated system.

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[Hewlett-Packard Co.]. The results were compared using statistical analytical methods and are shown in the attached Figure 1.

These results demonstrate a reduction in plasma triglyceride concentration of 41% in comparison to the placebo. In addition, the cholesterol levels showed a 9% reduction, the LDL levels showed a 7% reduction, and the HDL levels showed a 17% increase.

These data provide the basis for evaluating the effectiveness of the present invention in causing an increase in human serum HDL levels and a decrease in the levels of serum cholesterol, triglycerides, and low density lipoprotein (LDL).

EXAMPLE 2

The following example provides a preferred composition of the present invention. The composition is provided as two separate preparations: lozenge A (fish oil) and lozenge B (garlic, capsaicin, and rutin). The proper daily dosage is six of lozenge A and four of lozenge B (in other words, three of lozenge A and two of lozenge B taken twice daily for a total of ten lozenges).

20	Lozenge A	Ingredient	1000	Weight mg
		Fish Oil		1000 mg
	Lozenge B		700 m	ng
25		Garlic Powder Capsaicin Rutin lemon bioflavonoid parsley powder		487 mg 53 mg 27 mg 23 mg 110 mg

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EXAMPLE 3

The following example provides a preferred composition of the present invention. The composition is provided as two separate preparations: Lozenge A (fish oil) and Lozenge B (garlic, capsaicin, rutin). The proper dosage is six capsules of Lozenge A each day and four capsules of Lozenge B (in other words, three of lozenge A and two of lozenge B taken twice daily for a total of ten lozenges).

			Ingredient		Weight
10	Lozenge	Α		950	mg
			Fish Oil		950 mg
	Lozenge	В		700	mg
15	_		Garlic Powder Capsaicin Rutin		600 mg 50 mg 50 mg
				EXAMPLE	E 4

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The following example provides a preferred composition of the present invention. The composition is provided as a single preparation. The proper dosage is five capsules of the lozenge taken twice each day.

25	Ingredient fish oil* garlic powder rutin capsaicin lemon bioflavonoids parsley powder d-alpha tocopherol bee's wax lecithin gelatin	Weight 570 mg 194 mg 11 mg 21 mg 11 mg 38 mg 5 mg 75 mg 75 mg 255 mg
	purified water glycerin	10 mg 170 mg

fish oil in the form of 300:200 of EPA:DHA

Numerous modifications and variations of the present invention are included in the above-identified specification and are expected to be obvious to one of skill in the art. It is also intended that the present invention cover modifications and variations of the compositions and method for using them to accomplish their claimed uses within the scope of the appended claims and their equivalents.

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WE CLAIM:

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- A nutritional supplement comprising fish oil, garlic, rutin, and capsaicin.
- The nutritional supplement of claim 1, wherein the fish oil is in the form of a single fish oil lozenge.
 - 3. The nutritional supplement of claim 2, wherein the garlic, rutin, and capsaicin are in the form of a single garlic, rutin, and capsaicin lozenge.
- 4. The nutritional supplement of claim 1, wherein the fish10 oil, garlic, rutin, and capsaicin are in the form of a single
 lozenge.
 - 5. The nutritional supplement of claim 3, wherein the fish oil lozenge is between approximately 350 mg to approximately 650 mg.
- 6. The nutritional supplement of claim 5, wherein the fish oil lozenge is approximately 500 mg.
 - 7. The nutritional supplement of claim 3, wherein the garlic is between approximately 200 mg to approximately 700 mg, the rutin is between approximately 10 mg to approximately 150 mg, and the capsaicin is between approximately 20 mg to approximately 150 mg.
 - 8. The nutritional supplement of claim 7, wherein the fish oil is approximately 500 mg, the garlic is approximately 500 mg, the rutin is approximately 100 mg, and the capsaicin is approximately 100 mg.
 - 9. The nutritional supplement of claim 7, wherein the fish oil is approximately 500 mg, the garlic is approximately 275 mg, the rutin is approximately 135 mg, and the capsaicin is

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approximately 90 mg.

- 10. The nutritional supplement of claim 7, wherein the fish oil is approximately 600 mg, the garlic is approximately 200 mg, the rutin is approximately 10 mg, and the capsaicin is approximately 20 mg.
- 11. The nutritional supplement of claim 3, wherein the garlic, rutin, and capsaicin lozenge is between approximately 350 mg and approximately 650 mg.
- 12. The nutritional supplement of claim 7, wherein the garlic, rutin, and capsaicin lozenge is approximately 500 mg.
 - 13. The nutritional supplement of claim 3, wherein the total weight of the fish oil and garlic, rutin, and capsaicin lozenges is between approximately 700 mg and approximately 1,300 mg.
- 14. The nutritional supplement of claim 13, wherein the total weight of the fish oil and garlic, rutin, and capsaicin lozenges is approximately 1,000 mg.
 - 15. The nutritional supplement of claim 1, wherein the fish oil comprises between approximately 250 IU to approximately 350 IU EPA.
 - 16. The nutritional supplement of claim 15, wherein the fish oil comprises approximately 300 IU EPA.
 - 17. The nutritional supplement of claim 1, wherein the fish oil comprises between approximately 150 IU to approximately 250 IU DHA.
 - 18. The nutritional supplement of claim 17, wherein the fish oil comprises approximately 200 IU DHA.
 - 19. The nutritional supplement of claim 1, wherein the

garlic is in the form of garlic powder.

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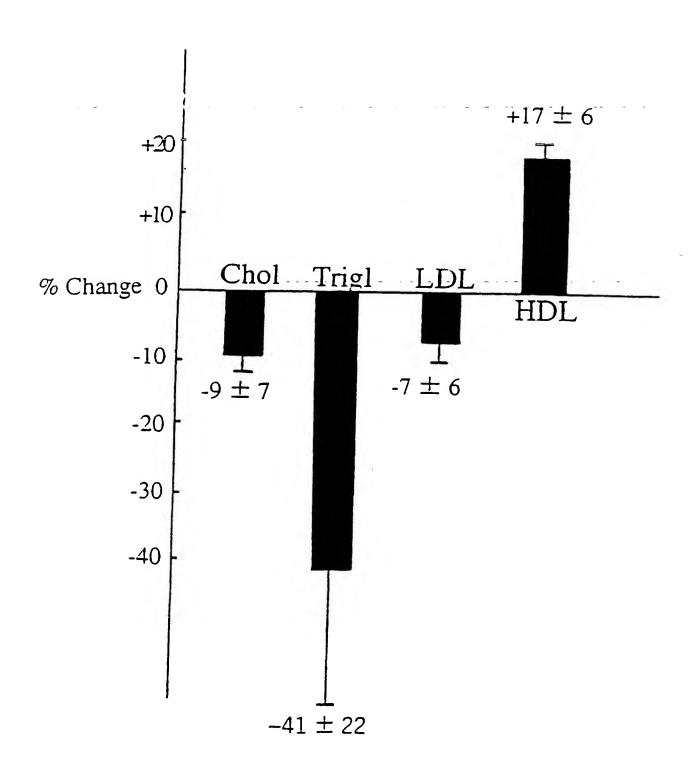
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- 20. A method of preparing the nutritional supplement of the present invention comprising admixing the fish oil, garlic, rutin, and capsaicin components with a suitable carrier.
- 21. A method of increasing the levels of HDL in human blood plasma comprising administering daily the nutritional supplement of claim 3 or claim 4.
- 22. A method of decreasing the levels of O-LDL, cholesterol, and triglycerides in human blood plasma comprising administering daily the nutritional supplement of claim 3 or claim 4.
- 23. The method of claim 21, wherein the daily dosage is comprised of from approximately 4 to approximately 8 fish oil lozenges together with from approximately 3 to approximately 5 garlic, rutin, and capsaicin lozenges.
- 24. The method of claim 22, wherein the daily dosage is comprised of from approximately 4 to approximately 8 fish oil lozenges together with from approximately 3 to approximately 5 garlic, rutin, and capsaicin lozenges.
- 25. The method of claim 23 or claim 24, wherein the daily dosage is comprised of approximately 6 fish oil lozenges together with approximately 4 garlic, rutin, and capsaicin lozenges.

Figure 1

Effect of Fish Oil/ Garlic on Lipid Profile



INTERNATIONAL SEARCH REPORT

International application No. PCT/US96/10500

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	LASSIFICATION OF SUBJECT MATTER		
IPC(6)	:A61K 35/78, 31/70, 31/20, 31/16 : :424/195.1; 514/27, 560, 627		
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	Contg. Omega-three Fatty Acid Thrombotic Illness And Lowerin	s Blood Chalanteral Laure III	
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